DEPARTMENT OF VETERANS AFFAIRS
Veterans Health Administration
Washington, DC 20420

Date: [DRAFT]

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Office of Research and Development Information Letter

Solicitation of Applications for the
Clinical Science Research and Development Service

PHARMACOGENOMIC ANALYSIS LABORATORY

1. **Introduction.** This Veterans Health Administration (VHA) Clinical Science Research and Development Service (CSRD) Information Letter announces the opportunity for investigators from Department of Veterans Affairs (VA) Medical Centers to compete for support to establish and implement a Pharmacogenomics Analysis Laboratory (PAL) for the systematic examination of pharmacogenomic data in therapeutic decision making. Research on pharmacogenomics is currently funded through established programs that solicit investigator-initiated research, such as Merit Review. Within CSRD, the Cooperative Studies Program (CSP) has been planning for integration of this research effort.

2. **Purpose.** The PAL will be dedicated to evaluating the clinical utility of pharmacogenomic data. The PAL will develop a comprehensive laboratory capable of developing and conducting pharmacogenomic tests for the express purpose of assessing the utility in both controlled clinical trials and well-designed observational studies. The PAL will be expected to work closely with the CSRD Service and especially with the CSP and Epidemiology Research Centers (ERICS), in developing appropriate “test menus” in support of ongoing and planned clinical trials and observational studies. The PAL will be expected to operate under the standards of the Clinical Laboratory Improvement Amendments of 1988 (CLIA88).

3. **Scope and Responsibilities.** The PAL will (1) comprehensively identify and review available research and clinical information relevant to the pharmacogenomic analysis of drugs specifically under investigation in CSP multi-site clinical trials, as well as other drugs that may be identified by the Director, CSRD and (2) develop, validate and implement within the laboratory such testing protocols as required to support the needs of the VA Genomic Medicine Program or CSP. The PAL will work with VA investigators to design studies that evaluate the clinical utility of pharmacogenomic testing prior to therapeutic decision making, and will also serve as an integral component of planning committees as new clinical trials are designed.

In addition, PAL scientists will be expected to work closely with members of the VA medical informatics, research, and laboratory medicine communities to develop approaches by which genomic information can be integrated into the electronic medical record for both treatment and research purposes.

The PAL must operate in accordance with CLIA88 and be certified by a deemed laboratory accreditation program within 2 years of commencing operation.

4. **Eligibility.** The Principal Investigator will serve as PAL Director. He/she must meet current ORD eligibility requirements. Current eligibility requirements are described in VHA Handbook 1200.15, Eligibility for VA Research Support, accessible on the VA web site at http://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=440. The VA Medical Center and the Veterans Integrated Services Network (VISN) must support the PAL application and agree to provide a minimum of 25% protected time (2/8ths) for the Director to coordinate PAL activities.

   The PAL Director must demonstrate appropriate expertise in clinical laboratory genetics, preferably through appropriate certification by a recognized medical specialty board. The Director should hold a certificate in Clinical Molecular Genetics or Molecular Genetic Pathology, although other certification will be considered. Strong evidence of the ability to work as a member of a cohesive team must be provided.

   It is also expected that additional scientific staff will commit all or a majority of their effort to the PAL. These scientists should contribute to and strengthen the PAL's capabilities, and their role should be clearly delineated in the application.

5. **Background.** The genetic makeup of an individual affects the propensity to develop disease, the response to medications and other treatment, and the likelihood of an unexpected or adverse reaction to a treatment that is safe and effective for most people. Advances in genetics give great promise that genetic information can be used to individualize patient treatment, but the impetus for "mass customization" of treatment requires that the fruits of the genome project be brought together with clinical information in an exceptionally effective way. By coupling genetic analysis with the electronic medical record, the VA will accelerate the timeframe with which the benefits of the genetic revolution can be brought to veterans to improve patient care at a reduced cost, especially by reducing the costs of the current trial-and-error approach to pharmacotherapy.

   Some of these benefits are imminent. Investigators from the University of Washington have recently shown that genetic variation in the gene CYP2C9 affects response to the drug warfarin, used to treat patients who have had clots in the legs or heart valve replacement. If not enough warfarin is given,

blood clots may develop, but if too much is given, a patient may bleed. Finding the right dose has been a trial and error procedure that can take weeks. Use of genetic information may reduce this timeframe to days, and at the same time, reduce the risk of an adverse event. Polymorphisms in cytochrome oxidase genes significantly affect drug metabolism and show promise for improving initial dosing. The Food and Drug Administration (FDA) has recently approved one test for identifying such polymorphisms.

VA is committed to developing the effective use of genetic information in both diagnosis and in therapeutic decision making. The PAL will advance this commitment by coordinating the systematic examination of pharmacogenetic data collected in ongoing and planned studies, and evaluating the utility for clinical decision making to improve patient care.

6. **Intent to Submit.** Information regarding intent to submit a proposal under this RFP is due February 21, 2005. The following information should be sent by electronic mail to vhacocenter@va.gov from the local VA research office:

   (a) PAL Director Name, Degree, and VA appointment (in eighths)
   (b) Proposed time commitment of the Director to the PAL
   (c) VA Medical Center
   (d) Title of Proposed Program
   (e) List of participating investigators

   A confirmation e-mail acknowledging receipt of intent to submit information will be sent from ORD and should be included as the last page of the full proposal when submitted.

7. **Proposal Preparation and Submission.** Applications are due May 1, 2006. Detailed instructions are provided in Attachment A.

8. **Review.** All proposals will be evaluated on the basis of scientific quality, rigor of the methodological approaches proposed, investigator qualifications, and relevance to the areas of interest and priorities identified in this announcement. Availability of matching funds from the medical center or VA nonprofit organization will also be considered. A special review committee will be formed for this evaluation, which may include scientific and/or administrative evaluations to assess a site's capacity for implementing the proposed program. Proposals that do not address the programmatic objectives outlined in this announcement or follow stated guidelines will not be accepted for review.

9. **Funding.** Proposals may request up to 2 years of funding. Generally, the maximum budget will be $600,000 for the first year, to support equipment acquisition and initial staffing and training, with a maximum of $225,000 in the second year. Funding after this time will be provided, as appropriate, through competitive Merit Review or CSP mechanisms as charge-backs.

If the PAL Director is eligible to receive salary, it may only be included in the budget if he/she is not already salaried from another VA source. Salaries for Title 38 employees will be provided only to a maximum of 2/8 effort.

The proposed program is expected to be appropriate and efficient, with all budget categories well justified. In planning budgets, applicants are reminded to adhere to ORD guidelines regarding allowable use of research funds for specific items. Appropriateness of the proposed budget will be evaluated by the review committee; the budget may be adjusted if not adequately justified or supported by the proposed research.

10. **Inquiries.** Please direct all questions regarding this RFP (areas of research investigation, eligibility, application preparation, funding, review, etc.) to Grant Huang, PhD at (202) 254-0496 or Terri Gleason, PhD at (202) 254-0498. E-mail inquiries may be directed to vhacocenter@va.gov.

Joel Kupersmith, MD
Chief Research and Development Officer

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